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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/208,619	12/08/98	HILLMAN J	PF-0229-1DIV

HM12/0524

LEGAL DEPARTMENT
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EXAMINER	
HARRIS, A	
ART UNIT	**PAPER NUMBER**
1642	9

DATE MAILED: 05/24/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/208,619	Hillman And Goll
Examiner	**Group Art Unit**
Alana M. Harris, Ph. D.	1642

☒ Responsive to communication(s) filed on *April 24, 2000.*

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claim

☒ Claim(s) *2-10 and 17-43* is/are pending in the applicat

Of the above, claim(s) *2-10, 19-31, and 34-43* is/are withdrawn from consideration

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *17, 18, 32, and 33* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☒ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____ .

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). 3, filed December 8, 1999.

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

1. Applicant's election with traverse of Group I (claim 1) in Paper No.6 (filed April 24, 2000) is acknowledged. The traversal is on the grounds that the invention encompassed by Groups I-VI are interrelated as to be capable of search of all claims and would not pose an undue burden on the Examiner. This is not found persuasive.

The argument that Groups I -VI are not independent and distinct inventions is not found persuasive for the reasons set forth in the restriction requirement (Paper No.5, mailed March 22, 1999). As to the question of burden of search, the claims of Groups I-VI are classified differently, necessitating different searches in the U.S. Patent shoes. Further, classification of subject matter is merely one indication of the burdensome nature of the search involved. The literature search, particularly relevant in this art, is not co-extensive and is much more important in evaluating the burden of search. Clearly different searches and issues are involved in the examination of each group. For these reasons the restriction requirement is deemed to be proper and is adhered to. Further, Groups IV-VI involve different method steps, which require additional searching.

The requirement is therefore made FINAL.

However, the policies set forth in the Commissioner's Notice of February 28, 1996 published on March 26, 1996 at 1184 O.G. 86 will be followed. Method claims limited to the scope of the allowable product claims will be rejoined and examined at the time the product claims are indicated as being allowable.

2. Claims 17-43 have been added.

Claims 1 and 11-16 have been canceled.

Claims 2-10 and 17-43 are pending.

Claims 2-10, 19-31 and 34-43, drawn to non-elected inventions are withdrawn from examination.

Claims 17, 18, 32 and 33 are examined on the merits.

Specification

3. The disclosure is objected to because of the following informality. A misspelled word, "protozan" instead of "protozoan" on page 25, line 9. Applicant is advised to review the entire specification for similar errors.

Appropriate correction is required.

Claim Rejections - 35 U.S.C. § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claim 17, 18, 32 and 33 are rejected under 35 U.S.C. 112, first paragraph, because the specification, does not reasonably provide enablement commensurate with the scope of the

claimed invention. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

a. Claim 32 is broadly drawn to "A pharmaceutical composition comprising an effective amount of polypeptide...". The specification while being enabling for a composition comprising a polypeptide of claim 1 and a pharmaceutically acceptable carrier, does not reasonably provide enablement for a "pharmaceutical composition" comprising these same components. Claims drawn to "pharmaceutical compositions" are broadly interpreted to read on compositions effective for use as *in vivo* human therapeutics. The polypeptide of the invention is completely uncharacterized functionally. The mere fact that it seems to be expressed in a wide variety of cells and tissues as stated in the specification, page 24 is not sufficient to establish that it plays a role in the pathology or etiology of diseases (i.e., AIDS, Crohn's disease and scleroderma) in these tissues. In the absence of an established role of the polypeptide in just the listed diseases and their affected tissues it is impossible to predict what if any therapeutic effect the administration of the polypeptide would have for the treatment of AIDS or scleroderma. The selection and development of such human therapeutics is art known to be highly unpredictable. The specification exemplifies no examples of the effective use of the effective use of the polypeptide as a pharmacological agent and no such uses are art known. This reasonably conjures the question as to how selective the expression of the claimed proteins clearly is. Could these claimed proteins reasonably be selective and specific in their application of detecting a marker for

just Crohn's disease or asthma assays/diagnoses when their expression can not be limited to just those tissue types? Accordingly, those skilled in the art cannot rely on this information to identify the expression of these polypeptides solely as specific markers. One skilled in the art would not know how to use the claimed compositions as the component polypeptide was not known prior to the applicant's invention. Its function is not known and is not disclosed in the specification. The "associated" protein claimed is not known to be useful for the treatment of scleroderma, asthma and/or cancer. Therefore, due to the unpredictability of therapeutics and the absence of any evidence concerning the effectiveness of the claimed pharmaceutical composition as a pharmacological agent, the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use with a reasonable expectation of success, the invention commensurate in scope with this claim. The association provides no guidance as to how the instant polypeptides can be employed as therapeutic nor a basis to predict their efficacy. The applicant is advised to amend the claim to delete the recitation of "pharmaceutical".

b. Claim 32 is broadly drawn to "...an effective amount...". The claimed invention is not described in such, full clear and concise exact terms to enable any person skilled in the art to make and use the same. The claim fails to state the function which is to be achieved by an "effective amount" and the specification provides no such guidance. One of skill in the art would not have a reasonable expectation of success in practicing the claimed invention and one skilled in the art would not be able to practice the claimed invention without undue experimentation.

6. Claims 17 and 18 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 17(c and d) is broadly drawn to a purified polypeptide comprising an amino sequence selected from a biologically-active fragment of the amino acid sequence of SEQ ID NO:1 and an immunogenic fragment of the amino acid sequence of SEQ ID NO:1. This claim is drawn to a polypeptide fragment that contains a small number of amino acid residues that is less than the 172 amino acids of SEQ ID NO:1, hence the claim is drawn to amino acid residues that minimally contain only portions of SEQ ID NO:1. Absent evidence to the contrary, each of the fragments is deemed to be an incomplete polypeptide, likewise it is clear that the partial sequences would not be the claimed polypeptide consisting of amino acid sequence of SEQ ID NO:1, nor function as the full length polypeptide is alleged. Thus, the claims are drawn to a large genus of molecules. In the case of small identified amino acid residues claimed with open language, the genus of polypeptides comprising only a partial sequence encompasses a variety of subgenera with widely varying attributes. The specification discloses only the structural features of one species, the polypeptide sequence of SEQ ID NO:1. The specification lacks information to lead one of skill in the art to understand that the applicant had possession of the broadly claimed invention at the time the instant application was filed. Applicant is referred to the interim guidelines

concerning compliance with the written description requirement of 35 U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 17, 18, 32 and 33 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. The recitations "naturally-occurring", 'biologically-active" and "immunogenic" in claim 17 are not clear. What functional properties are bestowed upon these designated sequences described by these terms?

b. The phrase "effective amount" in claim 32 is vague and indefinite when the claims fail to state the function which is to be achieved.

Claim Rejections - 35 U.S.C. § 101

9. Claims 17 and 18 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility, a credible or a well established utility.

The applicant has asserted several utilities for the claimed purified polypeptide and fragments. The specification asserts the following utilities for the claimed polypeptide, as well as fragments of the sequence: compositions for the diagnosis, prevention or treatment of cancer and disorders associated with fungal and parasitic infections, a marker to identify new antiprotozoal and antifungal agents, and in the manufacture of medicaments and diagnostics. However, these asserted utilities are not credible, specific or substantial for the broadly claimed polypeptide. Other that the sequence identification number, the specification provides no functional characterization of the polypeptide, no specific tissue distribution of the polypeptide and no specific disease state in which these proteins affect. The broadly claimed polypeptide is termed a novel human mitochondrial membrane protein (HuTIM17). This protein according to the specification, page 5 can be obtained from any species (i.e. bovine, equine or human) and from any source whether natural, synthetic or recombinant. This protein is also expressed in a wide variety of cells and tissues involved in mitochondrial protein transport. HuTIM17 has been suggested to prevent or treat infections by protozoan parasites, **but not limited to**, the *Leishmania, Trypanosoma* and *Plasmodia* for example, as well as cancer, AIDS and a host of other disorders affecting immunocompromised individuals. Consequently, there is no information that links expression of the claimed polypeptide to **any specific** tissue or disorder. Thus, the asserted utility of the claimed nucleic acids is not substantial, specific or credible.

Claims 17, 18, 32 and 33 are also rejected under 35 U.S.C., first paragraph. Specifically, since the claimed invention is not supported by either and substantial asserted utility or a well

established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Claim Rejections - 35 U.S.C. § 102

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

11. Claim 17 is rejected under 35 U.S.C. 102(b) as being anticipated by Accession Numbers P39515, Q02310, Maarse et al. (FEBS Letters 349:215-221, 1994, Reference #5 on IDS) and Ryan et al. (Mol. Biol. Cell 5:529-538, 1994, Reference #4 on IDS). Accession Numbers P39515, Q02310, Maarse et al. (see page 217, Figure 1B) and Ryan et al. (see page 532, Figure 3) disclose a purified polypeptide comprising an amino acid sequence that is a biologically-active fragment and an immunogenic fragment of the amino acid sequence of SEQ ID NO:1.

12. Claim 17 is rejected under 35 U.S.C. 102(e) as being anticipated by U.S. Patent #5,876,991 (filed Feb. 21, 1997). U.S. Patent #5,876,991 (see columns 85 and 86, Table 9)

discloses a purified polypeptide comprising an amino acid sequence that is a biologically-active fragment and an immunogenic fragment of the amino acid sequence of SEQ ID NO:1.

Claim Rejections - 35 U.S.C. § 103

13. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

14. Claim 32 is rejected under 35 U.S.C. 103(a) as being unpatentable over Accession Numbers P39515, Q02310, Maarse et al. (FEBS Letters 349:215-221, 1994, Reference #5 on IDS) and Ryan et al. (Mol. Biol. Cell 5:529-538, 1994, Reference #4 on IDS) and U.S. Patent #5,876,991, in view of Harlow and Lane (Antibodies, A Laboratory Manual, Cold Spring Harbor Laboratory, 1988). As previously discussed, the aforementioned references teach a purified polypeptide comprising a biologically-active fragment and an immunogenic fragment of amino acid sequence SEQ. ID. NO. 1. Accession Numbers P39515, Q02310, Maarse et al. (FEBS Letters 349:215-221, 1994, Reference #5 on IDS) and Ryan et al. (Mol. Biol. Cell 5:529-538, 1994, Reference #4 on IDS) and U.S. Patent #5,876,991 do not teach polypeptides comprised in a composition such as an adjuvant contained with saline, mineral oil or aluminum hydroxide.

Harlow and Lane teach the pharmaceutically acceptable diluent of pH neutral, phosphate buffered saline solution for the storage of polypeptides and the production of adjuvants. It would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to formulate a pharmaceutical composition comprising a carrier/excipient and the polypeptides of claim 1 in order to store the polypeptides in solution for the purpose of making an adjuvant. One of ordinary skill in the art would have been motivated to store the polypeptides in saline because Harlow and Lane teach that these components are necessary when producing an effective adjuvant. Moreover, one of ordinary skill in the art would have had a reasonable expectation of success in placing the polypeptides of claim 1 in a pharmaceutically acceptable carrier such as saline because this protocol is a standardly used immunological technique described in basic antibodies manual such as Harlow and Lane.

Because pharmaceutically acceptable carriers such as sterile saline solution and phosphate-buffered-saline solution were well known in the art, one of ordinary skill would have known how to formulate a pharmaceutical composition comprising a carrier/excipient and the instantly claimed polypeptides.

When the claim is directed to a product, the preamble or intended use is generally nonlimiting if the body of the claim is directed to an old composition and the preamble merely recites a property inherent in the old composition. [*Kropa v. Robie*, 88 USPQ 478, 480 - 81 (CCPA 1951); see also M.E.P.. 2111.02]. Thus, art which reads on a compound may also be

applied to pharmaceutical compositions consisting essentially of said compound and a suitable pharmaceutical carrier.

It has been held by the Court that a compound and a carrier are obvious, if it is obvious in the art to utilize a carrier with related compounds. See In re Rosicky, 125 USPQ 341 (CCPA 1960).

15. Claims 18 and 33 are free of the art.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Alana M. Harris whose telephone number is (703)306-5880. The examiner can normally be reached on Monday through Friday from 7:00 am to 3:30 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, can be reached on (703)308-3995. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703)308-0196.

Alana M. Harris, Ph.D.
Patent Examiner, Group 1642
May 20, 2000

NANCY A. JOHNSON, PH.D
PRIMARY EXAMINER